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accession number NP_619642, *Homo sapiens* taste receptor (TASR1) mRNA; as **Exhibit E**, a copy of the abstract from the scientific publication entitled "Human receptors for sweet and umami taste" (Li, et al., PNAS 99(7):4692-6, 2002).

AMENDMENT

In the claims:

Please cancel claims 4 and 5 without prejudice and without disclaimer, as being drawn to non-elected inventions. Please amend claims 1 and 2, so that the text of the amended claims reads as follows. Please add new claims 6 and 7.

1. (Amended) An isolated nucleic acid molecule comprising the nucleotide sequence of SEQ ID NO:1.

2.(Amended) An isolated nucleic acid molecule comprising a nucleotide sequence that:

(a) encodes the amino acid sequence shown in SEQ ID NO:2; and

(b) hybridizes under highly stringent conditions to the complement of the nucleotide sequence of SEQ ID NO: 1.

6.(New) An expression vector comprising a nucleic acid sequence encoding the amino acid sequence shown in SEQ ID NO: 2.

7.(New) A cell comprising the expression vector of Claim 6.

RESPONSE

I. Status of the Claims

Claims 4 and 5 have been cancelled without prejudice and without disclaimer, as being drawn to non-elected inventions. Claims 1 and 2 have been amended. New claims 6 and 7 have been added. Claims 1-3, 6 and 7 are therefore presently pending in the case. For the convenience of the Examiner, a clean copy of the pending claims is attached hereto as **Exhibit A**. In compliance with 37 C.F.R. § 1.121(c)(1)(ii), a marked up copy of the original claims is attached hereto as **Exhibit B**.

II. Support for the Claims

Claim 1 has been amended to further clarify the claim. Support for this claim can be found throughout the specification as originally filed, with particular support being found at least in Claim 1 and the sequence listing as originally filed.

Claim 2 has been amended to further clarify the claim, and to recite that the stringent hybridization conditions are highly stringent hybridization conditions. Support for this claim can be found throughout the specification as originally filed, with particular support being found at least in claim 1 as originally filed and at page 8, lines 12-18.

New Claim 6 has been added to more clearly claim aspects of the invention. Support for this claim can be found throughout the specification as originally filed, with particular support being found at least at page 17, line 31-page 18, line 3.

New claim 7 has been added to more clearly claim aspects of the invention. Claim 7 finds support throughout the specification as originally filed, with particular support being found at least at page 18, lines 3-10.

As the amendments to claims 1 and 2 and new claims 6 and 7 are fully supported by the specification and claims as originally filed, they do not constitute new matter. Entry therefore is respectfully requested.

III. Rejection of Claim 1 Under 35 U.S.C. § 112, Second Paragraph

The Action rejects Claims 1 and 2 under 35 U.S.C. § 112, second paragraph, as allegedly being indefinite for failing to particularly point out and distinctly claim the invention.

Specifically, the Action rejects Claim 1 as allegedly indefinite based on the use of the phrase "first disclosed" is unclear. While Applicants in no way agree with this assertion, Applicants respectfully submit that revised Claim 1 does not contain the phrase and thus Applicants submit that the rejection has been avoided and that Claim 1 is sufficiently definite, and respectfully request withdrawal of this rejection.

Specifically, the Action next rejects Claim 2 as allegedly indefinite based on the term "stringent hybridization conditions". While Applicants submit that the term is sufficiently definite, as a number of stringent hybridization conditions are defined in the specification and would be known to those of skill

in the art, solely in order to progress the case more rapidly toward allowance the claim has been revised to recite "highly stringent hybridization conditions". As the specification provides specific teaching regarding "highly stringent hybridization conditions", at least at page 8, lines 12-18. Applicants submit that revised Claim 2 even more clearly meets the requirements of 35 U.S.C. § 112, second paragraph. Applicants stress that "a claim need not 'describe' the invention, such description being the role of the disclosure". *Orthokinetics, Inc. v. Safety Travel Chairs, Inc.*, 1 USPQ2d 1081, 1088 (Fed. Cir. 1986). Based on the foregoing, Applicants submit that Claim 2 is sufficiently definite, and respectfully request withdrawal of this rejection.

IV. Rejection of Claims Under 35 U.S.C. § 101

The Action rejects claims 1-3 under 35 U.S.C. § 101, as allegedly lacking a patentable utility due to not being supported by a specific, substantial, and credible utility or, in the alternative, a well-established utility. Applicants respectfully traverse. The present invention has a number of substantial and credible utilities, not the least of which relates to polymorphisms identified in the sequences of the present invention described in the specification at page 7, line 27 - page 8, line 6.

The present application describes a novel G-protein coupled receptor (GPCR). Of the pharmaceutical products currently being market by the entire industry, 60% of these drugs target G-protein coupled receptors (Gurrath, 2001, Curr. Med. Chem. *8*:1257-1299). Given that more than half of the currently marketed drugs target proteins that are structurally (7TM proteins) and functionally (G-protein interaction) related to the presently described sequences, a preponderance of the evidence clearly weighs in favor of Applicants' assertion that the presently described sequences have a specific (the claimed GPCR proteins are taste receptors encoded by a specific locus on the human genome), credible, and well-established utility.

As set forth by the Federal Circuit, "(t)he threshold of utility is not high: An invention is 'useful' under section 101 if it is capable of providing some identifiable benefit." *Juicy Whip Inc. v. Orange Bang Inc.*, 51 USPQ2d 1700 (Fed. Cir. 1999) (citing *Brenner v. Manson*, 383 U.S. 519, 534 (1966)). Additionally, the Federal Circuit has stated that to violate § 101 the claimed invention "must be totally incapable of achieving a useful result." *Brooktree Corp. v. Advanced Micro Devices, Inc.*, 977 F.2d 1555, 1571 (Fed. Cir. 1992), emphasis added. *Cross v. Iizuka* (224 USPQ 739 (Fed. Cir.

1985)) states "any utility of the claimed compounds is sufficient to satisfy 35 U.S.C. § 101". *Id* at 748, emphasis added. Indeed, the Federal Circuit recently emphatically confirmed that "anything under the sun that is made by man" is patentable *(State Street Bank & Trust Co. v. Signature Financial Group Inc.*, 47 USPQ2d 1596, 1600 (Fed. Cir. 1998), citing the U.S. Supreme Court's decision in *Diamond vs. Chakrabarty*, 206 USPQ 193 (S.Ct. 1980)).

As the protein of the instant invention belongs to a family of compounds with a common, well established specific and substantial utility, the Federal Circuit's ruling in *In re Brana,* (34 USPQ2d 1436 (Fed. Cir. 1995), "*Brana*") is completely on point. In *Brana*, the Federal Circuit admonished the P.T.O. for confusing "the requirements under the law for obtaining a patent with the requirements for obtaining government approval to market a particular drug for human consumption". *Brana* at 1442. The Federal Circuit went on to state:

> At issue in this case is an important question of the legal constraints on patent office examination practice and policy. The question is, with regard to pharmaceutical inventions, what must the applicant provide regarding the practical utility or usefulness of the invention for which patent protection is sought. This is not a new issue; it is one which we would have thought had been settled by case law years ago.

Brana at 1439, emphasis added. The choice of the phrase "utility or usefulness" in the foregoing quotation is highly pertinent. The Federal Circuit is evidently using "utility" to refer to rejections under 35 U.S.C. § 101, and is using "usefulness" to refer to rejections under 35 U.S.C. § 112, first paragraph. This is made evident in the continuing text in *Brana*, which explains the correlation between 35 U.S.C. §§ 101 and 112, first paragraph. The Federal Circuit concluded:

> FDA approval, however, is not a prerequisite for finding a compound useful within the meaning of the patent laws. Usefulness in patent law, and in particular in the context of pharmaceutical inventions, necessarily includes the expectation of further research and development. The stage at which an invention in this field becomes useful is well before it is ready to be administered to humans. Were we to require Phase II testing in order to prove utility, the associated costs would prevent many companies from obtaining patent protection on promising new inventions, thereby eliminating an incentive to pursue, through research and development, potential cures in many crucial areas such as the treatment of cancer.

Brana at 1442-1443, citations omitted.

The Examiner states that a substantial utility amounts to more than a starting point for further research and investigation (Action at page 5-6). For even if, *arguendo*, further research might be required in certain aspects of the present invention, this does not preclude a finding that the invention has utility, as set forth by the Federal Circuit's holding in *Brana*, which clearly states, as highlighted in the quote above, that "pharmaceutical inventions, necessarily includes the expectation of <u>further research and development</u>" (*Brana* at 1442-1443, emphasis added). In assessing the question of whether undue experimentation would be required in order to practice the claimed invention, the key term is "undue", not "experimentation". *In re Angstadt and Griffin*, 190 USPQ 214 (CCPA 1976). The need for some experimentation does not render the claimed invention unpatentable. Indeed, a considerable amount of experimentation may be permissible if such experimentation is routinely practiced in the art. *In re Angstadt and Griffin, supra*; *Amgen, Inc. v. Chugai Pharmaceutical Co., Ltd.*, 18 USPQ2d 1016 (Fed. Cir. 1991). As a matter of law, it is well settled that a patent need not disclose what is well known in the art. *In re Wands*, 8 USPQ 2d 1400 (Fed. Cir. 1988).

As just <u>one</u> example of utility of the present nucleotide sequences, Applicants point out that, as taught in the specification as originally filed the claimed polynucleotide sequences can be used to track the expression of the genes encoding the described proteins. In particular, the specification describes how the described sequences can be represented using a gene chip format to provide a high throughput analysis of the level of gene expression. Such "DNA chips" clearly have utility, as evidenced by hundreds of issued U.S. Patents, as exemplified by U.S. Patent Nos. 5,445,934, 5,556,752, 5,744,305, 5,837,832, 6,156,501 and 6,261,776. Evidence of the "real world" <u>substantial</u> utility of the present invention is provided by the fact that there is an entire industry established based on the use of gene sequences or fragments thereof in a gene chip format. Perhaps the most notable gene chip company is Affymetrix. However, there are many companies which have, at one time or another, concentrated on the use of gene sequences or fragments, in gene chip and non-gene chip formats, for example: Agilent Technologies, Gene Logic, ABI-Perkin-Elmer, HySeq and Incyte. In addition, one such company, Rosetta Inpharmatics, was viewed to have such "real world" value (net equity value of the transaction was $620 million) that it was acquired by large pharmaceutical company, Merck & Co., for significant sums of money. The "real world" <u>substantial</u> industrial utility of gene sequences or fragments would, therefore, appear to be widespread and well established. The sequences of the

present invention describe a novel gene encoding a GPCR and provide a unique identifier of the corresponding gene. Such gene chips clearly have utility, as evidenced by hundreds of issued U.S. Patents, such as U.S. Patent Nos. 5,445,934, 5,556,752, 5,744,305, 5,837,832, 6,156,501 and 6,261,776. The present nucleotide sequences clearly encode human GPCRs, as detailed throughout the specification. The specification also teaches that GPCRs are associated with a wide variety of cellular functions, and as such, that GPCR interacting proteins have been subject to intense scrutiny as potential drug targets. Therefore, as the present sequences are specific markers of the human genome, and such specific markers are targets for the discovery of drugs that are associated with human disease, those of skill in the art would instantly recognize that the present nucleotide sequences would be an ideal, novel candidate for assessing gene expression using such gene chips. Clearly, compositions that enhance the utility of such DNA chips, such as the presently claimed nucleotide sequences, must in themselves be useful. Thus, the present claims clearly meet the requirements of 35 U.S.C. § 101.

Although Applicants need only make one credible assertion of utility to meet the requirements of 35 U.S.C. § 101 (*Raytheon v. Roper*, 220 USPQ 592 (Fed. Cir. 1983); *In re Gottlieb*, 140 USPQ 665 (CCPA 1964); *In re Malachowski*, 189 USPQ 432 (CCPA 1976); *Hoffman v. Klaus*, 9 USPQ2d 1657 (Bd. Pat. App. & Inter. 1988)), as a further example of the utility of the presently claimed polynucleotides, the Examiner is respectfully reminded that only a minor percentage of the genome actually encodes exons, which in-turn encode amino acid sequences. The presently claimed polynucleotide sequences provide biologically validated empirical data (*e.g.*, showing which sequences are transcribed, spliced, and polyadenylated) that *specifically* define that portion of the corresponding genomic locus that actually encodes exon sequence. Equally significant is that the claimed polynucleotide sequences define how the encoded exons are actually spliced together to produce an active transcript (*i.e.*, the described sequences are useful for functionally defining exon splice-junctions). The Applicants respectfully submit that the practical scientific value of expressed, spliced, and polyadenylated mRNA sequences is readily apparent to those skilled in the relevant biological and biochemical arts. For further evidence in support of the Applicants' position, the Examiner is requested to review, for example, section 3 of the Venter *et al.* article (Science, 2001, *291*:1304 *at* pp. 1317-1321, including Fig. 11 at pp.1324-1325), which demonstrates the significance of expressed sequence information in the structural analysis of genomic data. The presently claimed polynucleotide sequences

define biologically validated sequences that provide a unique and specific resource for mapping genome essentially as described in the Venter *et al.* article Thus, the present claims clearly meet the requirements of 35 U.S.C. § 101.

Furthermore, persons of skill in the art, as well as thousands of venture capitalists and investors, readily recognize the utility, both scientific and commercial, of genomic data in general, and specifically human genomic data. Billions of dollars have been invested in the human genome project, resulting in useful genomic data (see, *e.g.*, Venter *et al.*, 2001, Science *291*:1304). The results have been a stunning success, as the utility of human genomic data has been widely recognized as a great gift to humanity (see, *e.g.*, Jasny and Kennedy, 2001, Science *291*:1153). Clearly, the usefulness of human genomic data, such as the presently claimed nucleic acid molecules, is substantial and credible (worthy of billions of dollars and the creation of numerous companies focused on such information) and well-established (the utility of human genomic information has been clearly understood for many years).

The legal test for utility simply involves an assessment of whether those skilled in the art would find any of the utilities described for the invention to be credible or believable. According to the Examination Guidelines for the Utility Requirement, if the applicant has asserted that the claimed invention is useful for any particular purpose (i.e., it has a "specific and substantial utility") and the assertion would be considered credible by a person of ordinary skill in the art, the Examiner should not impose a rejection based on lack of utility (66 Federal Register 1098, January 5, 2001).

As evidence of the credibility of Applicants assertion that the present invention is an GPCR. Applicants submit a sequence comparison between SEQ ID NO: 2 and NP_619642 (**Exhibit C**), which has been annotated by third party scientists, wholly unaffiliated with Applicants, as encoding *Homo sapiens* taste receptor (TASR1) mRNA (NP_619642:**Exhibit D**). SEQ ID NO 2 of the present invention and NP_619642 are nearly identical. NP_619642 identifies a truncated form of the present invention, which is clearly encoded by the same genetic locus. Thus NP_619642 could represent a fragment or an isoform resulting of the use of an alternate promoter. In any case those of skill in the art have identified the sequence as encoding a human GPCR, *Homo sapiens* taste receptor (TASR1). This clearly supports Applicant's assertion that those of skill in the art would recognize the present invention as a GPCR and a taste receptor.

Given this clear evidence that those of skill in the art would recognize the present invention as a GPCR and a human taste receptor, whose function is described in part by the scientific publication entitled "Human receptors for sweet and umami taste" (Li, et al., PNAS 99(7):4692-6, 2002, Abstract included as **Exhibit E**). Clearly, there can be no question that Applicants' asserted utility for the described sequences is "credible." Applicants have thus supplied evidence supporting their assertion that those of skill in the art would recognize that the sequences of the present invention encode a G protein-coupled receptor, in particular that of a human taste receptor. Applicant's assertion also supports a "well-established" utility in that a person of ordinary skill in the art would immediately appreciate why the invention is useful based on its identity as a GPCR, a well known family of proteins with well established ,specific and substantial utility. In contrast, the Examiner has provided no evidence of record indicating that those of skill in the art would not recognize the sequences of the present invention encode a G protein-coupled receptor. As such, the scientific evidence clearly establishes that Applicants have described an invention whose utility is in full compliance with the provisions of 35 U.S.C. § 101, and the Examiner's rejection should be withdrawn.

Additionally, methods similar to those of the present invention were used to identify the GPCR of issued U.S. Patent 6,043,052. Issued U.S. Patents are presumed to be valid and to meet the requirements of 35 U.S.C. §§ 101, 102, 103 and 112, specifically, that they have utility, are novel, non-obvious, are enabled, meet the written description requirements and particularly point out and distinctly claim the invention. Therefore, the Applicants' assertion that the described GPCR is in fact a GPCR is also supported by issued U.S. Patent 6,043,052, as well as the plethora of other GPCR patents that the office has issued. For example, the specific and substantial utility of human GPCRs is evidenced by the fact that they are the subject of the above mentioned U.S. Patent No. 6,043,052 which discloses polynucleotides encoding a novel GPCR and U.S. Patent Nos. 5,891,646 and 6,110,693, both of which disclose and claim methods for detecting GPCR activity *in vivo* and *in vitro*, methods for assaying GPCR activity, and methods of screening for GPCR ligands, GPCR kinase activity, components that interact with GPCR regulatory processes and constructs useful in such methods. The issuance of these U.S. patents clearly indicates that GPCR polynucleotides have utility and that such utilities were sufficiently specific and substantial to warrant the issuance of U.S. patents directed to methods used to identify and characterize GPCRs. The teachings of these patentable

disclosures are directly applicable to the present invention (GPCR polynucleotides) and are evidence that those skilled in the art recognize the specific and substantial utility of GPCRs. In light of the issuance of U.S. Patent No. 6,043,052 on polynucleotides encoding a novel GPCR, Applicants respectfully submit that the present application, which also describes polynucleotides encoding a novel GPCR, describes an invention with specific and substantial utility fully compliant with 35 U.S.C. § 101.

The utility of the present invention is further supported by Applicant's assertion that the present invention has utility in the field of forensic biology, among others, is recognized in the Action which states (Page 7, second paragraph) that "one of skill in the art would appreciate that there may exist polymorphisms in the disclosed sequences, this amounts to nothing more than an invitation to the skilled artisan to try to find such polymorphisms if they exist." This statement is clearly inaccurate as the specification identifies several polymorphisms in both the nucleic acid and amino acid sequences of the present invention and the Action recognizes this on page 12, second paragraph. Thus clearly polymorphisms exist and no search by another skilled artisan is necessary as the polymorphisms of the present invention have been clearly identified in the specification (page 7, line 27 and 28). The specification identifies several polymorphisms within SEQ ID NO:1. For example, depending on whether the nucleic acid at position 320 of SEQ ID NO: 1 is a C or a T, the amino acid at position 107 of SEQ ID NO:2, can be either a S or F; an A or a G polymorphism at position 1,114 of SEQ ID NO: 1, results in a corresponding A or T at the amino acid at position 372 of SEQ ID NO:2; and a silent C or T transition exists at nucleotide 2526 of Seq ID NO:1.

These polymorphisms provide significant and specific utility as taught in the specification. Such polymorphisms have significant and specific utility in, *intra alia*, the fields of forensic science and human population biology. Such polymorphisms can also be used as specific markers useful, for example, in identifying human remains, determining human group migration patterns by identifying descendants of a specific group and in addition clearly the polymorphisms of the present invention has significant and specific utility in resolving issues of paternity. Further, Applicants submit that these utilities are not only credible, but well established and known to those of skill in the art. As such polymorphisms are the basis for forensic analysis, paternity identification and population biology studies, which are undoubtedly "real world" utilities, the present sequences must in themselves be useful. In and of themselves each of these polymorphisms, including the silent ones, has significant and specific utility, the specificity of this

utility is only amplified by the presence of more than one polymorphism which can arise in various combinations. It is also important to note that the presence of more useful polymorphic markers for such analysis would not mean that the present sequences lack utility.

Therefore, for each of the foregoing reasons, and because it is clear that it has been established that it is far more likely than not that a person skilled in the art would consider credible the utilities asserted by the applicant for the claimed invention, Applicants submit that the rejection of claims 1-3 under 35 U.S.C. § 101 have been overcome, and respectfully request that the rejection be withdrawn.

V. Rejection of Claims Under 35 U.S.C. § 112, First Paragraph

The Action rejects claims 1-3 under 35 U.S.C. § 112, first paragraph, since allegedly one skilled in the art would not know how to use the invention, as the invention allegedly is not supported by a specific, substantial, and credible utility or a well-established utility. Applicants respectfully traverse.

Applicants submit that claims 1-3 have been shown to have "a specific, substantial, and credible utility", as detailed in section IV above. Applicants therefore request that the rejection of claims 1-3 under 35 U.S.C. § 112, first paragraph, be withdrawn.

VI. Rejection of Claims 1 Under 35 U.S.C. § 112, First Paragraph

The Action rejects claim 1 under 35 U.S.C. § 112, first paragraph, as allegedly containing subject matter which is not described in the specification ins such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention. This rejection is based on the assertion that "claim 1 encompasses a vast genus of polynucleotides" (Action at page 8, last paragraph). Applicants in no way agree with the Examiner's position that original Claim 1 lacks enablement. However, Applicants submit that this rejection has been avoided by revision of Claim 1 to read on the full length molecule. Therefore, Applicants respectfully request that the rejection of claim 1 under 35 U.S.C. § 112, first paragraph, be withdrawn.

The Action next rejects claim 1 under 35 U.S.C. § 112, first paragraph, as allegedly containing subject matter which was not described in the specification in such a way as to reasonably convey to

one skilled in the relevant art that the inventor(s), at the time the application was filed had possession of the claimed invention. Applicants respectfully disagree.

The skilled artisan would easily recognize 24 contiguous nucleic acids derived from any of the nucleic acid sequences described in the sequence listing and would also know how to use a nucleic acid molecule that comprises 24 contiguous bases of nucleic acid sequence of SEQ ID NO:1. In fact, Applicants note that the entire DNA gene chip industry is based on the use of 24 or more contiguous bases of nucleic acid sequence. Therefore, Applicants submit that those of skill in the art would be able to make and use the present invention.

However, this traverse has been rendered moot due to Applicants amendment of claim 1 to read on the full length molecule. Thus, Applicants respectfully submit that this rejection has been avoided and withdrawal is respectfully requested.

VII. Rejection of Claims Under 35 U.S.C. § 102(b)

The Action rejects claim 1 under 35 U.S.C. § 102(b), as being anticipated by WO 00/06592, Zuker *et al.*, February 10 , 2000. While Applicants do not necessarily agree with the present rejection, as claim 1 has been amended to recite the complete nucleotide sequence of SEQ ID NO:1, which is neither taught nor suggested by WO 00/06592, Zuker *et al.* (February 10 , 2000), Applicants submit that the rejection of claim 1 under 35 U.S.C. § 102(b) has been thus avoided, and respectfully request withdrawal of the rejection.

VIII. Conclusion

The present document is a full and complete response to the Action. In conclusion, Applicants submit that, in light of the foregoing remarks, the present case is in condition for allowance, and such favorable action is respectfully requested. Should Examiner Brannock have any questions or comments, or believe that certain amendments of the claims might serve to improve their clarity, a telephone call to the undersigned Applicants' representative is earnestly solicited.

Respectfully submitted,

October 17, 2002

Date

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24231
PATENT TRADEMARK OFFICE

Exhibit A

Clean Version of the Pending Claims in U.S. Patent Application Ser. No. 09/819,946

1.(Amended) An isolated nucleic acid molecule comprising the nucleotide sequence of SEQ ID NO:1.

G_1

2.(Amended) An isolated nucleic acid molecule comprising a nucleotide sequence that:

(a) encodes the amino acid sequence shown in SEQ ID NO:2; and

(b) hybridizes under highly stringent conditions to the complement of the nucleotide sequence of SEQ ID NO: 1.

3. An isolated nucleic acid molecule comprising a nucleotide sequence that encodes the amino acid sequence shown in SEQ ID NO:2.

G_2

6.(New) An expression vector comprising a nucleic acid sequence encoding the amino acid sequence shown in SEQ ID NO: 2.

7.(New) A cell comprising the expression vector of Claim 6.

Exhibit B

Marked Up Version of Amended Claims in U.S. Patent Application Ser. No. 09/819,946

1.(Amended) An isolated nucleic acid molecule comprising [at least 22 contiguous bases of] the nucleotide sequence [first disclosed in] of SEQ ID NO:1.

2.(Amended) An isolated nucleic acid molecule comprising a nucleotide sequence that:

(a) encodes the amino acid sequence shown in SEQ ID NO:2; and

(b) hybridizes under highly stringent conditions to the complement of the nucleotide sequence of SEQ ID NO: 1.

3. An isolated nucleic acid molecule comprising a nucleotide sequence that encodes the amino acid sequence shown in SEQ ID NO:2.

4.(Cancelled) An isolated nucleic acid molecule comprising a nucleotide sequence that encodes the amino acid sequence shown in SEQ ID NO:4.

5.(Cancelled) An isolated nucleic acid molecule comprising a nucleotide sequence that encodes the amino acid sequence shown in SEQ ID NO:6.

6.(New) An expression vector comprising a nucleic acid sequence encoding the amino acid sequence shown in SEQ ID NO: 2.

7.(New) A cell comprising the expression vector of Claim 6.

```
 FASTA searches a protein or DNA sequence data bank
 version 3.3t05 March 30, 2000
Please cite:
 W.R. Pearson & D.J. Lipman PNAS (1988) 85:2444-2448

/tmp/fastaCAALIaqn6: 838 aa
 >hNGPR_28_SEQ ID_2 Taste Receptor
 vs  /tmp/fastaDAAMIaqn6 library
searching /tmp/fastaDAAMIaqn6 library

   763 residues in    1 sequences

FASTA (3.34 January 2000) function [optimized, BL50 matrix (15:-5)] ktup: 2
 join: 38, opt: 26, gap-pen: -12/ -2, width:  16
 Scan time:  0.034
The best scores are:                                      opt
gi|20162558|ref|NP_619642.1| taste receptor, type  ( 763) 5129

>>gi|20162558|ref|NP_619642.1| taste receptor, type 1, m  (763 aa)
 initn: 4955 init1: 2699 opt: 5129
Smith-Waterman score: 5129;  99.345% identity in 763 aa overlap (79-838:1-763)

       50        60        70        80        90       100
hNGPR_ GCLQVRHRPEVTLCDRSCSFNEHGYHLFQAMRLGVEEINNSTALLPNITLGYQLYDVC-D
                                    :::::::::::::::::::::::::::: :
gi|201                              MRLGVEEINNSTALLPNITLGYQLYDVCSD
                                            10        20        30

      110       120       130       140       150       160
hNGPR_ SANVYATLRVLSLPGQHHIELQGDLLHYSPTVLAVIGPDSTNRAATTAALLSPFLVPMIS
       ::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::
gi|201 SANVYATLRVLSLPGQHHIELQGDLLHYSPTVLAVIGPDSTNRAATTAALLSPFLVPMIS
              40        50        60        70        80        90

       170       180       190       200       210       220
hNGPR_ YAASSETLSVKRQYPSFLRTIPNDKYQVETMVLLLQKFGWTWISLVGSSDDYGQLGVQAL
       ::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::
gi|201 YAASSETLSVKRQYPSFLRTIPNDKYQVETMVLLLQKFGWTWISLVGSSDDYGQLGVQAL
             100       110       120       130       140       150

       230       240       250       260       270       280
hNGPR_ ENQATGQGICIAFKDIMPFSAQVGDERMQCLMRHLAQAGATVVVVFSSRQLARVFFESVV
       ::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::
gi|201 ENQATGQGICIAFKDIMPFSAQVGDERMQCLMRHLAQAGATVVVVFSSRQLARVFFESVV
             160       170       180       190       200       210

       290       300       310       320       330       340
hNGPR_ LTNLTGKVWVASEAWALSRHITGVPGIQRIGMVLGVAIQKRAVPGLKAFEEAYARADKEA
       :::::::::::::::::::::::::::::::::::::::::::::::::::::::::::: :
gi|201 LTNLTGKVWVASEAWALSRHITGVPGIQRIGMVLGVAIQKRAVPGLKAFEEAYARADKXA
             220       230       240       250       260       270

       350       360       370       380       390       400
hNGPR_ PRPCHKGSWCSSNQLCRECQAFM-HTMPKLKAFSMSSAYNAYRAVYAVAHGLHQLLGCAS
       :::::::::::::::::::::: :::::::::::::::::::::::::::::::::::::
gi|201 PRPCHKGSWCSSNQLCRECQAFMAHTMPKLKAFSMSSAYNAYRAVYAVAHGLHQLLGCAS
             280       290       300       310       320       330

       410       420       430       440       450       460
hNGPR_ GACSRGRVYPWQLLEQIHKVHFLLHKDTVAFNDNRDPLSSYNIIAWDWNGPKWTFTVLGS
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          ::::::::::::::::::::::::::::::::::::::::::::::::::::::::::
gi|201 GACSRGRVYPWQLLEQIHKVHFLLHKDTVAFNDNRDPLSSYNIIAWDWNGPKWTFTVLGS
               340       350       360       370       380       390

        470       480       490       500       510       520
hNGPR_ STWSPVQLNINETKIQWHGKDNQVPKSVCSSDCLEGHQRVVTGFHHCCFECVPCGAGTFL
       ::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::
gi|201 STWSPVQLNINETKIQWHGKDNQVPKSVCSSDCLEGHQRVVTGFHHCCFECVPCGAGTFL
               400       410       420       430       440       450

        530       540       550       560       570       580
hNGPR_ NKSDLYRCQPCGKEEWAPEGSQTCFPRTVVFLALREHTSWVLLAANTLLLLLLLGTAGLF
       ::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::
gi|201 NKSDLYRCQPCGKEEWAPEGSQTCFPRTVVFLALREHTSWVLLAANTLLLLLLLGTAGLF
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        590       600       610       620       630       640
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       ::::::::::::::::::::::::::::::::: :::::::::::::::::::::::::
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        650       660       670       680       690       700
hNGPR_ LTVRSFQLIIIFKFSTKVPTFYHAWVQNHGAGLFVMISSAAQLLICLTWLVVWTPLPARE
       ::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::
gi|201 LTVRSFQLIIIFKFSTKVPTFYHAWVQNHGAGLFVMISSAAQLLICLTWLVVWTPLPARE
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        710       720       730       740       750       760
hNGPR_ YQRFPHLVMLECTETNSLGFILAFLYNGLLSISAFACSYLGKDLPENYNEAK-VTFSLLF
       :::::::::::::::::::::::::::::::::::::::::::::::::::: :::::::
gi|201 YQRFPHLVMLECTETNSLGFILAFLYNGLLSISAFACSYLGKDLPENYNEAKCVTFSLLF
               640       650       660       670       680       690

         770       780       790       800       810       820
hNGPR_ NFVSWIAFFTTASVYDGKYLPAANMMAGLSSLSSGFGGYFLPKCYVILCRPDLNSTEHFQ
       ::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::
gi|201 NFVSWIAFFTTASVYDGKYLPAANMMAGLSSLSSGFGGYFLPKCYVILCRPDLNSTEHFQ
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         830
hNGPR_ ASIQDYTRRCGST
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gi|201 ASIQDYTRRCGST
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838 residues in 1 query   sequences
763 residues in 1 library sequences
 Scomplib [version 3.3t05 March 30, 2000]
 start: Wed Oct 16 10:50:30 2002 done: Wed Oct 16 10:50:31 2002
 Scan time:  0.034 Display time:  0.866

Function used was FASTA
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☐ 1: NP_619642. taste receptor, t...[gi:20162558] Links

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DEFINITION  taste receptor, type 1, member 1 [Homo sapiens].
ACCESSION   NP_619642
VERSION     NP_619642.1  GI:20162558
DBSOURCE    REFSEQ: accession NM_138697.1
KEYWORDS    .
SOURCE      Homo sapiens.
  ORGANISM  Homo sapiens
            Eukaryota; Metazoa; Chordata; Craniata; Vertebrata; Euteleostomi;
            Mammalia; Eutheria; Primates; Catarrhini; Hominidae; Homo.
REFERENCE   1  (residues 1 to 763)
  AUTHORS   Makalowska,I., Sood,R., Faruque,M.U., Hu,P., Robbins,C.M.,
            Eddings,E.M., Mestre,J.D., Baxevanis,A.D. and Carpten,J.D.
  TITLE     Identification of six novel genes by experimental validation of
            GeneMachine predicted genes
  JOURNAL   Gene 284 (1-2), 203-213 (2002)
  MEDLINE   21888635
   PUBMED   11891061
REFERENCE   2  (residues 1 to 763)
  AUTHORS   Li,X., Staszewski,L., Xu,H., Durick,K., Zoller,M. and Adler,E.
  TITLE     Human receptors for sweet and umami taste
  JOURNAL   Proc. Natl. Acad. Sci. U.S.A. 99 (7), 4692-4696 (2002)
  MEDLINE   21927605
   PUBMED   11917125
COMMENT     PROVISIONAL REFSEQ: This record has not yet been subject to final
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      181 lmrhlaqaga tvvvvfssrq larvffesvv ltnltgkvwv aseawalsrh itgvpgiqri
      241 gmvlgvaiqk ravpglkafe eayaradkxa prpchkgswc ssnqlcrecq afmahtmpkl
      301 kafsmssayn ayravyavah glhqllgcas gacsrgrvyp wqlleqihkv hfllhkdtva
      361 fndnrdplss yniiawdwng pkwtftvlgs stwspvqlni netkiqwhgk dnqvpksvcs
      421 sdcleghqrv vtgfhhccfe cvpcgagtfl nksdlyrcqp cgkeewapeg sqtcfprtvv
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Revised: July 5, 2002.

1: Proc Natl Acad Sci U S A 2002 Apr 2;99(7):4692-6

Human receptors for sweet and umami taste.

Li X, Staszewski L, Xu H, Durick K, Zoller M, Adler E.

Senomyx, Inc., 11099 North Torrey Pines Road, La Jolla, CA 92037, USA.

The three members of the T1R class of taste-specific G protein-coupled receptors have been hypothesized to function in combination as heterodimeric sweet taste receptors. Here we show that human T1R2/T1R3 recognizes diverse natural and synthetic sweeteners. In contrast, human T1R1/T1R3 responds to the umami taste stimulus l-glutamate, and this response is enhanced by 5'-ribonucleotides, a hallmark of umami taste. The ligand specificities of rat T1R2/T1R3 and T1R1/T1R3 correspond to those of their human counterparts. These findings implicate the T1Rs in umami taste and suggest that sweet and umami taste receptors share a common subunit.

PMID: 11917125 [PubMed - indexed for MEDLINE]